UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,443	02/22/2006	Volety Srinivas	595222000100	4273

25226 7590 02/06/2007

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
TSAY, MARSHA M	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,443	SRINIVAS ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-18 are pending and currently under examination.

Priority: The benefit date is December 30, 2003, for the purpose of prior art.

Specification

The disclosure is objected to because of the following informalities: on page 1, the priority data needs to be updated with a cross-reference paragraph to related applications.

Appropriate correction is required.

Claim Objections

Claims 1-2, 5-18 are objected to because of the following informalities: the term "crystalline" should be corrected to "crystallin"; in claim 1(c), there should be a "the" inserted between "in presence"; in claims 7-8, the term "enhance" should be corrected to "enhances"; in claim 9, the term "maybe" should be corrected to "may be"; in claims 15-16, there should be a "the" inserted between "in presence". Appropriate correction is required.

All claims are replete with grammatical errors and should be corrected accordingly, e.g., in claim 1, the terms "a biological compatible" should be corrected to "biologically compatible"; in claim 1(a) "convention methods" should be corrected to "conventional methods", etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for enhancing molecular chaperone activity of α-crystallin with Arg.Hcl, does not reasonably provide enablement for enhancing molecular chaperone activity of mutant αA-crystallin with Arg.Hcl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which mutants of α-crystallin function in the same way as the wild-type protein. Thus there could be thousands of variants which contain substitutions, deletions, additions etc. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which derivatives or fragments were active.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by

weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are myriad substitutions, deletions or insertions to choose from. The amount of guidance in the specification is zero with regard to which amino acids in α-crystallin are essential for activity. Minimal examples are present of mutant α-crystallin proteins. The nature of the invention is such that many different proteins that are substantially similar to α-crystallin may or may not have biological activity. The state of the prior art is that even proteins that are 99% similar to the wild-type protein are at times not fully active. The relative level of skill in this art is very high. The predictability as to what substantially similar protein will have which activity is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1(a) recites by convention(al) methods (as described in reference 24). This part should be deleted because if the methods are conventional and known in the art then it is not necessary to state this. Claim 1(b) recites reacting α-crystallin in the presence of phosphate buffer pH 7.4 with Arg.HCl. The term "reacting" should be replaced with "mixing" because no reaction per se occurs between α-crystallin and Arg.HCl. Additionally, it is unclear what the reaction components are in claim 1(b), i.e. α-crystallin + Arg.HCl + insulin, α-crystallin + Arg.HCl + ζ-crystallin, α-crystallin + insulin, and/or α-crystallin + ζ-crystallin. Additional clarification is required. For examination purposes, it is assumed that claim 1(b) is directed to a reaction of α-crystallin with Arg.HCl, insulin, and DTT only. Claim1 should recite "Arg.HCl" during the first instance when Arginine Chloride is recited. Claim 1 recites DTT. The claim should specifically define DTT is dithiothreitol.

Claim 2 is redundant to claim 1 because Arg.HCl inherently binds to the peptide backbone of α-crystallin.

Claim 4 is rejected because of reciting a range dwithin a range, i.e. broad limitation followed by a narrow limitation. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim,

and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 4 recites a narrower range limitation for the broad recitation that is recited in the parent claim, i.e. claim 3. The claim recites a narrower range and/or limitation for the Arg.HCl concentration.

Claim 6 is improper because it does not further limit claim 5. Claim 5 recites a chaperone activity of about 95% while claim 6 recites an activity of about 90%.

Similarly, claims 8, 16, 18 are also improper because they are not more limiting than claims 7, 15, and 17, respectively.

Claim 9 recites selected from group comprising of. This phrase should be amended to "selected from the group ~~comprising~~ consisting of." Further, the claim recites related compounds. It is unclear what the related compounds are.

Claims 12-13 use the language "subtle" and "significant" changes. The terms "subtle" and "significant" render the claims indefinite. The terms "subtle" and "significant" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Additionally, claims 12-13 are redundant to claim 1. The changes in the tertiary and quaternary structure occur by inherency in claim 1. Claim 13 should recite "α-crystallin is reduced to ~360 kDa."

Claim 14 recites the limitation "mutant αA-crystallin " in the claim. There is insufficient antecedent basis for this limitation in the claim and its parent claim.

Claims 15-16 recite the limitation "mutant αB-crystallin " in the claim. There is insufficient antecedent basis for this limitation in the claims and its parent claim. Claims 15-16 recite protection of mutant αB-crystallin is about 80% or 70% in presence of Arg.HCl. The claims are indefinite because it is unclear what the protection is.

Claims 2-8, 10-11, 14, 17-18 are included in this rejection because they are dependent on the above claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

February 2, 2007

M. Monshipouri
MARYAM MONSHIPOURI, PH.D.
PRIMARY EXAMINER